AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method of ~~determining~~ establishing an alpha-2B-adrenergic receptor function ~~by detecting a polymorphism at a polymorphic site in a polynucleotide encoding an alpha-2B-adrenergic receptor molecule, the method~~ comprising:

a. obtaining an isolated ~~sample of a~~ polynucleotide ~~encoding an~~ that encodes said alpha-2B-adrenergic receptor, ~~molecule comprising SEQ ID NO: 1 or 2 or a fragment~~ or a complement thereof, or a fragment thereof, or a complement of said fragment, that includes nucleotides 901 to 909 of SEQ ID NO: 1, or nucleotides 901 to 909 of SEQ ID NO: 2, or their complements~~the polynucleotide~~;

b. detecting in ~~the sample a~~ said isolated polynucleotide the presence or absence of a deletion polymorphism ~~at a polymorphic site, wherein the polymorphic site is located at,~~ said deletion polymorphism exclusively consisting of the deletion of nucleotide positions 901 to 909 of SEQ ID NO: 1 ~~or 2 or a complement thereof~~; and

c. establishing that a ligand-binding function of said alpha-2B-adrenergic receptor is reduced if said deletion polymorphism is present as compared to said ligand-binding function if said deletion polymorphism is absent ~~correlating the polymorphism to an alpha-2B-adrenergic receptor function, thereby determining the function~~.

2. (Currently Amended) A method according to claim 1, wherein said detecting comprises a hybridization step ~~the polynucleotide comprises SEQ ID NO: 3 or 4, or a complement thereof, at the polymorphic site~~.

3-15 (Cancelled)

16. (Currently Amended) A method of ~~ge~~phenotyping an individual ~~by genotyping a polynucleotide encoding an alpha-2B-adrenergic receptor molecule from a sample of the individual~~, comprising:

establishing the alpha-2B-adrenergic receptor function according to claim 1, thereby determining phenotype of said individual from whom said isolated polynucleotide was obtained.

a. ~~isolating from the individual a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide;~~

b. ~~subjecting the polynucleotide to an incubation with at least one oligonucleotide, the at least one oligonucleotide having a nucleotide sequence that is complementary to a region of the polynucleotide, and which, when hybridized to the region permits the identification of the nucleotides present at a polymorphic site of the polynucleotide, wherein the incubation is under conditions sufficient to allow specific hybridization to occur between complementary nucleic acid molecules;~~

c. ~~permitting hybridization to occur; and~~

d. ~~identifying the polymorphic site to obtain the genotype of the individual, wherein the polymorphic site comprises a polymorphism comprising an insertion or deletion of 9 nucleotides exactly at nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2, wherein the at least one oligonucleotide is selected from the group consisting of~~

~~5' AAAGCCCCACCATGGTCGGGT 3' (SEQ ID NO: 14);~~

~~5' CTGATCGCCAAACGAGCAAC 3' (SEQ ID NO: 15);~~

~~5' AAAAACGCCAATGACCACAG 3' (SEQ ID NO: 16);~~

~~5' AGAAGGAGGGTGTTTGTGGGG 3' (SEQ ID NO: 19);~~

~~5' ACCTATAGCACCCACGCCCCT 3' (SEQ ID NO: 20);~~

~~5' GGCCGACGCTCTTGTCTAGCC 3' (SEQ ID NO: 21);~~

~~5' CAAGGGGTTCCTAAGATGAG 3' (SEQ ID NO: 22); and complementary sequences thereof.~~

17. (Currently Amended) The method according to claim ~~1~~62, further comprising amplifying the deletion polymorphism of the polynucleotide prior to the hybridization.

18. (Cancelled)

19. (Currently Amended) The method according to claim ~~1~~62, wherein said hybridization ~~the specific hybridization~~ is selected from the group consisting of southern blot, dot blot, reverse dot blot, northern blot, and allele-specific oligonucleotide hybridization.

20. (Currently Amended) The method according to claim ~~1~~62, wherein the ~~at least one~~ oligonucleotide is labeled with a label selected from the group consisting of radiolabel, fluorescent label, bioluminescent label, chemiluminescent label, nucleic acid label, hapten label, and enzyme label.

21. (Currently Amended) The method according to claim ~~1~~62, wherein said detecting comprises a step selected from the group consisting of ~~the identity of the polymorphic site is determined by~~ dideoxy sequencing, restriction digestion, allele-specific polymerase reaction, single-stranded conformational polymorphism analysis, genetic bit analysis, temperature gradient gel electrophoresis; ligase chain reaction, or ligase/polymerase genetic bit analysis, ~~or~~ and random amplification of DNA.

22. (Currently Amended) The method according to claim ~~1~~62, wherein the ~~at least one~~ oligonucleotide is from about 10 to about 50 nucleotides in length.

23. (Withdrawn) A method of detecting a polymorphic site in a sample to determine alpha-2B-adrenergic receptor function, comprising:

a. obtaining the sample having an alpba-2B-adrenergic receptor molecule comprising amino acid SEQ ID NO: 7 or 8 or fragment thereof and

b. detecting in the sample the polymorphic site at amino acid positions 294 to 309 of SEQ ID NO: 7 or 8.

24. (Withdrawn) A method according to claim 23, wherein the polymorphic site comprises SEQ ID NO: 9 or 10.

25. (Withdrawn) A method according to claim 23, wherein the polymorphic site is an insertion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 7.

26. (Withdrawn) A method according to claim 27, wherein the polymorphic site is a deletion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 8.

27. (Withdrawn) A method of detecting a polymorphic site to determine alpha-2B-adrenergic receptor function, comprising:

a. obtaining a sample having an alpha-2B-adrenergic receptor molecule comprising amino acid SEQ ID NO: 7 or 8 or fragment thereof;

b. contacting the sample with an antibody specifically reactive with the polymorphic site at amino acid positions 294 to 309 of SEQ ID NO: 7 or 8; and

c. detecting in the sample a complex formed between the antibody and amino acid positions 294 to 309 of SEQ ID NO: 7 or 8.

28. (Withdrawn) A method according to claim 27, wherein the polymorphic site is an insertion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 7.

29. (Withdrawn) A method according to claim 27, wherein the polymorphic site is a deletion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 8.

30-44. (Cancelled)

45. (Withdrawn) A method of predicting an individual's response to an agonist or antagonist, comprising:

a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement of the polynucleotide from the individual;

b. detecting in the sample a polymorphic site comprising nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 or fragment or complement thereof; and

c. correlating the polymorphic site to a predetermined response thereby predicting the individual's response to the agonist or antagonist.

46. (Withdrawn) A method according to claim 45, wherein the alpha-2B adrenergic receptor molecule comprises SEQ ID NOS. 7 or 8 or fragment thereof.

47. (Withdrawn) A method according to claim 45, wherein the agonist is an alpha-2B adrenergic receptor agonist.

48. (Withdrawn) A method according to claim 45, wherein the antagonist is an alpha-2B adrenergic receptor antagonist.

49. (Withdrawn) A method according to claim 47, wherein the alpha-2B adrenergic receptor agonist is an agonist selected from the group consisting of epinephrine, norepinephrine, clonidine, oxymetazoline, guanabenz, UK14304, BHT933 and combinations thereof.

50. (Withdrawn) A method according to claim 48, wherein the alpha-2B adrenergic receptor antagonist is an antagonist selected from the group consisting of yohimbine, prazosin, ARC 239, rauwolscine, idazoxan, tolazoline, phentolamine and combinations thereof.

51. (Withdrawn) A method according to claim 45, wherein the predetermined response to the agonist or antagonist is correlated to adenyly cyclase, MAP kinase activity, phosphorylation or inositol phosphate levels.

52. (Withdrawn) A method according to claim 45, wherein the individual is homozygous for SEQ ID NO: 2 and exhibits a decreased response to the alpha-2B adrenergic receptor agonist.

53. (Withdrawn) A method according to claim 45, wherein the individual's response is desensitization to the agonist or antagonist,

54. (Withdrawn) A method according to claim 47, wherein the individual's response is desensitization to the alpha 2B-aadrenergic receptor agonist.

55. (Withdrawn) A method for selecting an appropriate pharmaceutical composition to administer to an individual having a disease associated with an alpha-2B adrenergic receptor molecule, comprising:

a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement of the polynucleotide from the individual;

b. detecting in the sample a polymorphic site comprising nucleotide positions 901 to 909 of SEQ ID NO:1 or 2 or fragment or complement thereof; and

c. selecting the appropriate pharmaceutical composition based on the polymorphic site present.

56. (Withdrawn) A method of claim 55, wherein the disease is a cardiovascular disease, a central nervous system disease or combinations thereof

57. (Withdrawn) A method according to claim 55, wherein the alpha-2B-adrenergic receptor molecule comprises SEQ ID NO.7 or 8 or fragment thereof.

58. (Withdrawn) A method according to claim 55, wherein the pharmaceutical composition is an alpha-2B-adrenergic receptor agonist or antagonist.

59. (Withdrawn) A method according to claim 58, wherein the alpha-2B-adrenergic receptor agonist is an agonist selected from the group consisting of epinephrine, norepinephrine, clonidine, oxymetazoline, guanabenz, UK14304, BHT933, and combinations thereof.

60. (Withdrawn) A method according to claim 58, wherein the alpha 2B adrenergic receptor antagonist is an antagonist selected from the group consisting of yohimbine, prazosin, ARC 239, rauwolscine, idazoxan, tolazoline, phentolamine and combinations thereof.

61. (Withdrawn) A method according to claim 58, wherein the appropriate pharmaceutical composition to administer is correlated to adenyly cyclase, MAP kinase, phosphorylation or inositol phosphate activity.

62. (Withdrawn) A method according to claim 55, wherein the individual is homozygous for SEQ ID NO: 2 and exhibits a decreased response to the alpha 2B adrenergic receptor agonist.

63. (Currently Amended) A method of ~~determining~~ establishing an alpha-2B-adrenergic receptor function ~~by detecting a polymorphism at a polymorphic site in a polynucleotide encoding an alpha 2B adrenergic receptor molecule, the method~~ comprising::

a. obtaining an isolated ~~sample of a~~ polynucleotide ~~encoding an~~ that encodes said alpha-2B-adrenergic receptor ~~molecule, wherein the polynucleotide, or a fragment~~ or a complement thereof, ~~comprises SEQ ID NO: 1 or 2~~ or a fragment thereof, or a complement of said fragment, that includes nucleotides 901 to 909 of SEQ ID NO: 1, or nucleotides 901 to 909 of SEQ ID NO: 2, or their complements~~the polynucleotide~~;

b. indirectly detecting in ~~the sample the~~ said isolated polynucleotide the presence or absence of a deletion polymorphism ~~at a polymorphic site, wherein the polymorphic site is located at~~, said deletion polymorphism exclusively consisting of the deletion of nucleotide positions 901 to 909 of SEQ ID NO: 1 ~~or 2 or a complement thereof~~; and

c. establishing that a ligand-binding function of said alpha-2B-adrenergic receptor is reduced if said deletion polymorphism is present as compared to said ligand-binding function if said deletion polymorphism is absent ~~correlating the polymorphism to a predetermined alpha 2B adrenergic receptor function, thereby determining the function~~.

64. (Withdrawn) A method of detecting a polymorphic site in a sample to determine alb 2B-adrenergic receptor function; comprising:

a. obtaining the sample having an alpha 2B-adrenergic receptor molecule comprising amino acid SEQ ID NO: 7 or 8 or fragment thereof; and

b. indirectly detecting in the sample the polymorphic site at amino acid positions 294 to 309 of SEQ ID NO: 7 or 8.

65. (Currently Amended) The method of ~~determining~~ establishing alpha-2B-adrenergic receptor function ~~by detecting a polymorphism at a polymorphic site in a polynucleotide encoding an alpha-2B-adrenergic receptor molecule~~ as recited in claim 1, wherein the function established further comprises mediation of adenylyl cyclase; MAP kinase; G protein receptor interaction; inositol phosphate; phosphorylation; receptor desensitization; and combinations thereof.

66. (Previously Presented) The method as recited in claim 65 wherein the function comprises phosphorylation.

67. (Currently Amended) The method as recited in claim 66, wherein the phosphorylation comprises agonist promoted ~~phposphorlyation~~ phosphorylation by G-protein coupled receptor kinases.